REMARKS

With entry of this amendment, claims 12-21 are pending in the application. Claims Claims 1-11 were previously withdrawn from consideration in response to a Restriction Requirement, with traverse and reservation to pursue the subject matter of the withdrawn claims in a related application. Claims 1-10, 12-15 and 18-21 have been amended for clarity and to correct typographical errors. All of the amendments herein are fully supported by the disclosure, and no new matter has been added to the application.

No fees are believed to be due in connection with the filing of this Amendment after Final Rejection other than the fee for a one month extension of time. However, should any additional fees be deemed necessary, the Commissioner is hereby authorized to deduct any necessary fees from Deposit Account No. 50-1050.

I. Patentability Under 35 USC § 103

The Office continues to reject claims 12-21 under 35 USC § 103(a) as allegedly unpatentable over Media Release (November 4, 2002) in view of Hirsh et al. (US 2003/0035839 A1), for essentially the same reasons as set forth in the prior Office Action issued by the Office in this case.

Applicants respectfully traverse the foregoing ground of rejection and submit that the subject matter of claims 12-21 is neither disclosed nor suggested by the cited references, either alone or in combination—based on the facts and reasoning set forth herein below, and as presented in the prior Amendment submitted by Applicants in this case, and in view of the entire record in this application.

A. The Cited References are Insufficient to Render the Claimed Invention Obvious

When properly considered, it is clear that the references cited by the Office are insufficient to render the claimed invention obvious.

The claims under consideration are directed to "a pharmaceutical oral unit dosage form" comprising two compartments, in which the active ingredient (ocinaplon or a pharmaceutically acceptable salt thereof) is in rapid release form in one compartment and sustained release form in the other compartment. Thus, in order to render the present claims obvious, the cited references must render this two compartment oral unit dosage form obvious.

The first reference, Media Release (November 4, 2002), simply discloses a study examining the effect of a controlled release form of ocinaplon, administered at a dose of 240 mg/day in two doses or 180 mg/day in three doses, for the treatment of generalized anxiety

disorders. There is no disclosure or suggestion in the reference of the two compartment oral unit dosage form of the present invention. As specifically noted by the Office, "Media Release does not teach two separate compartments each containing ocinaplon with specific amounts with rapid release in first compartment and sustained release in second compartment with hydrophilic polymeric matrix...." (Office Action, p. 4) As such, the record in the instant application fails to establish any direct suggestion or "practical" motivation in the prior art that would have led a person of ordinary skill in the art to develop the instantly claimed technology for delivering ocinaplon to treat anxiety.

The second reference, Hirsh et al. (US 2003/0035839) is similarly deficient. This reference discloses a pharmaceutical composition containing an outer layer for administering a pharmaceutically active ingredient intraorally (that is, by sublingual or buccal absorption through the mucous membranes of the mouth) and a second portion within the outer layer containing a pharmaceutically active ingredient for oral ingestion and subsequent absorption. There is no disclosure in Hirsh et al. of a two compartment oral unit dosage form of the present invention or any disclosure that the pharmaceutical composition for both intraoral administration and oral ingestion can be adapted or utilized only for oral ingestion.

Furthermore, as previously noted by Applicants, Hirsh et al. does not even indicate that ociniplon can be utilized in the pharmaceutical composition disclosed therein. Rather, the reference simply presents laundry lists of about 26 classes of drugs which are stated to be useful for both intraoral administration and oral injestion, about 167 specific compounds which are stated to be useful for intraoral administration and about 241 specific compounds which are stated to be useful for oral ingestion. Indeed, there are no working examples demonstrating that any of the listed classes of drugs or specific drugs can be successfully used in a pharmaceutical composition for both intraoral administration and oral ingestion, much less a two compartment oral dosage form such as the oral unit dosage form of the present invention. This position is contrary to fundamental principals in the art--that drugs of different classes, and even drugs within a particular class, exhibit widely divergent and highly unpredictable biological activities and pharmacokinetic properties. Based on these principals, it is not scientifically reasonable to interpret such vague and unfounded teachings as provided by Hirsh et al. as allegedly describing and placing into the hands of the public such unpredictable technology, spanning so vast a breadth of subject matter, as advocated by the Office.

Further contrary to the Office's position, Hirsh et al. provides no working examples of any kind of "anxiolytic" formulation. Rather, the examples of Hirsh et al. are limited to

combinations of (example 1) analgesics; (example 2) hypnotics; (example 3) anti-migraine drugs; (example 4) antihistamine/decongestant drugs; and (example 5) analgesics.

In addition, Hirsh et al. actually teaches away from the subject matter of the current invention, in that all of the working examples provided by Hirsh et al. of a "two portion" (outer layer and inner core) dosage forms are comprised of two separate drugs, which are each delivered in a separate phase of a distinct, bi-phasic delivery modality.

Applicants respectfully submit that these distinct descriptions teach directly away from providing a "two portion" dosage form for a single drug, and most certainly do not practically teach nor suggest such a two portion dosage form as an obvious modification of Media Release (teaching only a "controlled release" delivery mode).

Further in this context, the record is also deficient to support the proposed modification of Media Release (i.e., to employ a two portion dosage form), on the basis that "Media Release II (R & D Focus Drug News 2 Dec 2002; made of record with Office Action) similarly cites positive phase two results for "an immediate release formulation of ocinaplon". The Office provides no basis for distinguishing the cited Media Release (relating to "controlled release" ocinaplon), and Media Release II (relating to immediate release ocinaplon), that would evince a preference to investigate and develop controlled release ocinaplon dosage forms rather than immediate release ocinaplon dosage forms, or motivation to develop a two compartment oral dosage form for administration of ociniplon.

Finally, given the failure of Hirsh et al. to disclose or suggest a two compartment oral dosage form such as the oral unit dosage form of the present invention, it is clear that Media Release (November 4, 2002) read in view of Hirsh et al. (US 2003/0035839 A1) also does not disclose or suggest such a two compartment oral dosage form for administration of ociniplon.

Because the foregoing remarks establish that the instant rejection of the claims is improper, Applicants decline to address the more specific bases of the rejection set forth by the Office. Nonetheless, Applicants respectfully submit that the record is likewise deficient for failure to evince that "[t]he amounts of active agent (ocinaplon) to be used in each portion, the pharmaceutical carriers (e.g., lactose), and the particle size are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and each portion can be formulated with [the] same active agent contained therein...." (Office Action, p. 5) Here, it is likewise apparent that the blanket assertions by the Office (e.g., alleging that essentially all dosages for all drugs, in all conceivable dosage forms including two portion dosage forms, is within the knowledge of the ordinarily skilled pharmacologist) are unsupported by actual evidence in the record, and are contrary to fundamental principles of pharmacology.

B. The Applicable Case Law Supports the Patentability of the Present Invention

The position taken by the Office to support this rejection is inconsistent with established case law and constitutes, at best, an "obvious to try" rejection. In *In re O'Farrell*, 7 USPQ2d 1673 (Fed. Cir. 1990), the Court of Appeals for the Federal Circuit discussed the impropriety of "obvious to try" rejections, stating:

> The admonition that "obvious to try" is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been obvious to try would have been to vary all possible parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art either gave no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. (*Id.* at 1681, citations omitted)

In the present case, Hirsch et al. simply gives a laundry list of disparate compound classes and compounds of different chemical structures and physiochemical properties with no indication of what conditions might be used to successfully create a composition for both intraoral administration and oral ingestion, much less a composition for oral injestion only. In other words, it is clear that Hirsh et al. fail to provide sufficient direction as to what conditions might be successful for a particular class of compound or for a particular compound, such as ociniplon. Consequently, at best, Hirsh et al. represents an "invitation to experiment." (*In re Eli Lilly & Co.*, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990))

CONCLUSION

In view of the foregoing, Applicants believe that all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at (206) 381-3300.

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Respectfully submitted,

Jeffrey J. King, Esq.
Attorney for Applicant
Registration No. 38,515
BLACK LOWE & GRAHAM PLLC
701 Fifth Avenue – Suite 4800
Seattle, WA 98104
Telephone: (206) 381-3300
Facsimile: (206) 381-3301